IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| Appl. No. | : | 10/579,229 |
| Applicant | : | Vasso Apostolopoulos et al. |
| Filed | : | April 6, 2007 |
| TC/A.U. | : | 1635 |
| Examiner | : | Kimberly Chong |
| Docket No. | : | 3489-103 |
| Customer No. | : | 06449 |
| Confirmation No. | : | 1201 |

Director of the United States Patent
and Trademark Office
P.O. Box 1450
Alexandria, Virginia 22313-1450

**RESPONSE TO RESTRICTION REQUIREMENT**

In an Office Action dated August 8, 2008, the examiner of the above-referenced patent application asserted that the claims of the application are directed to more than one invention and that the groups of inventions are not so linked as to form a single general inventive concept under PCT Rule 13.1, on the basis that there is not a technical relationship among the inventions involving one or more of the same or corresponding special technical features. Accordingly, she has required that Applicants elect a single invention to which the claims will be restricted.

More specifically, the examiner has divided the claims into the following groups:

Group I: claims 1-14 and 18-20, drawn to a compound comprising a conjugate of a polynucleotide or

oligonucleotide molecule, a carrier comprising at least one aldehyde group and an optional linker, wherein the carrier is a hormone.

Group II: claims 1-14 and 18-20, drawn to a compound comprising a conjugate of a polynucleotide or oligonucleotide molecule, a carrier comprising at least one aldehyde group and an optional linker, wherein the carrier is an enzyme;

Group III: claims 1-14 and 18-20, drawn to a compound comprising a conjugate of a polynucleotide or oligonucleotide molecule, a carrier comprising at least one aldehyde group and an optional linker, wherein the carrier is a cytokine;

Group IV: claims 1-20, drawn to a compound comprising a conjugate of a polynucleotide or an oligonucleotide, a carrier comprising an aldehyde and an optional linker, wherein the carrier is a carbohydrate polymer;

Group V: claims 38-49, drawn to a compound comprising a conjugate of a polynucleotide or oligonucleotide, a carrier comprising an aldehyde and an optional linker, wherein the carrier is reduce mannan;

Group VI: claim 21, drawn to a method for cell-specific delivery of a polynucleotide or oligonucleotide to a target

cell of a subject comprising administering the compounds of claims 1-20;

Group VII: claims 22-27, drawn to a method for inducing an immune response to an antigen or epitope wherein the immune response is primarily a CD8+ type of immune response and the carrier is a hormone;

Group VIII: claims 22-27, drawn to a method for inducing an immune response to an antigen or epitope wherein the immune response is primarily a CD8+ type of immune response and the carrier is an enzyme;

Group IX: claims 22-27, drawn to a method for inducing an immune response to an antigen or epitope wherein the immune response is primarily a CD8+ type of immune response and the carrier is a cytokine;

Group X: claims 22-30, drawn to a method for inducing an immune response to an antigen or epitope wherein the immune response is primarily a CD8+ type of immune response and the carrier is a carbohydrate polymer; and

Group XI: claims 31-37, drawn to a method for inducing an immune response to an antigen or epitope wherein the immune response is primarily a CD8+ type of immune response.

This restriction requirement is traversed.

As an initial point, Applicants wish to point out to the examiner that a Preliminary Amendment was filed with the application on May 12, 2006, in which original claims 1-49 were canceled in favor of new claims 50-98. The new claim set was submitted to correct improper multiple dependent claims. In the discussion below, when Applicants refer to particular claim(s) it will be by the new number, followed by the corresponding number of the original claim set.

Turning now to the substance of the Action, the Applicants first wish to note that in the International Search Report (ISR) issued on the international (PCT) application from which the present application is derived (a copy of which is attached), the International Searching Authority (ISA) made no finding of a lack of unity of invention and, indeed, searched all of the present claims.

In addition, with regard to the reference the examiner cited as support for his position, Sasaki et al., *Eur. J. Immunol.* 27:3121-3129 (1997), Applicants respectfully submit that the examiner may not have focused on the fact that the "compound" recited in the present claims is a conjugate of a polynucleotide or oligonucleotide molecule with a carrier (the term "conjugate" is defined in the paragraph bridging pages 10 and 11). In contrast, the Sasaki et al document discloses a non-conjugated

mixture of DNA (particularly, an immunogenic DNA encoding gp160 of HIV-1) and mannan-coated diC14-amidine (as an adjuvant). The examiner's attention is directed to section 2.2 of the reference, where it is stated that the "mixtures were ... administered to mice." Furthermore, it should be noted that the authors suggest, from page 3128, that the mannan-coated diC14-amidine forms a small granule with a core occupied by the immunogenic DNA. In view of this distinction between the teachings of the reference and the subject matter of the present claims, Applicants submit that the claims of Groups I - XI are, in fact, unified by a "special technical feature," namely, a conjugate of a polynucleotide or oligonucleotide molecule with a carrier.

In addition, and notwithstanding the above, Applicants respectfully assert that the claims of Groups I - IV and VII - X are unified by a further "special technical feature," namely, the use of a carrier comprising at least one aldehyde group. This effectively means that the carrier is in oxidized form and, as is stated at page 4, lines 10-15, the use of an oxidized carrier surprisingly elicited a "primarily CD8+ immune response." The Sasaki et al. reference makes absolutely no mention or suggestion of the use of an oxidized carrier comprising at least one aldehyde group. It should be noted that in section 2.2 of the reference there is no mention of a step of oxidizing the mannan.

Thus, at most, the claims should only need to be restricted to the claims of Groups I - IV and VII - X.

In order to be fully responsive to the Office Action, however, Applicants acknowledge that they must elect a group for examination purposes in the event that the restriction requirement is made final. Applicants thus hereby elect the claims of Group IV, claims 50-69(1-20) as directed to a compound comprising a conjugate of a polynucleotide or oligonucleotide and a carbohydrate polymer carrier such as oxidized mannan, for initial prosecution on the merits. Applicants submit that, when these product claims are found to be allowable, it would be appropriate for the process claims of the application (i.e. claim 70 (21), directed to a method for cell-specific delivery of a polynucleotide or oligonucleotide molecule, and claims 71-79 (22-30), directed to a method of inducing an immune response) be rejoined to the application provided that the claims processes include all of the limitations of the broadest allowable product claim.

In addition to the restriction requirement, the examiner has required election of species. Applicants hereby elect the following species:

(i) with regard to claims 56, 57, 85, 86 and 92-94 (7, 8, 36, 37 and 43-45) and the requirement for an election from the

species of "an antigen, polytope peptide, enzyme or hormone," Applicants elect "an antigen;"

(ii) with regard to claims 58 and 95 (9 and 46) and the requirement for an election from "antisense RNA, catalytic RNA or siRNA," Applicants elect "siRNA;" and

(iii) with regard to claims 68, 69, 84 and 85 (19, 20, 48 and 49) and the requirement for an election from the linkers, "polycation linker, PLL, PEI, dendrimers or cationic lipids," Applicants elect "polycation linker."

Applicants respectfully submit that the claims of the application are in condition for allowance.


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# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)



| Applicant's or agent's file reference | FOR FURTHER ACTION | see Form PCT/ISA/220 as well as, where applicable, item 5 below. |
|---|---|---|
| MTO 03 13746995 | | |
| International application No. | International filing date *(day/month/year)* | (Earliest) Priority Date *(day/month/year)* |
| **PCT/AU2004/001564** | 12 November 2004 | 12 November 2003 |

Applicant

THE AUSTIN RESEARCH INSTITUTE et al

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II).

3. ☐ **Unity of invention is lacking** (See Box No. III).

4. With regard to the **title,**

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings,**

a. the figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

**INTERNATIONAL SEARCH REPORT**

International application No.
**PCT/AU2004/001564**

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. [7]: C12N 15/13, A61K 48/00, A61P 31/12, 31/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
STN On-line File MEDLINE, CA, WPIDS, BIOSIS, #Keywords: Mannan, Polysaccharide, Carbohydrate, DNA, RNA, ?Nucleotide, Oxid?, Conjugat?

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X, Y | STRYDOM, S. et. al., " Studies on the transfer of DNA into cells through use of avidin-polylysine conjugates complexed to biotinylated transferrin and DNA", Journal of Drug Targeting, (1993) 1 (2) 165-74. See page 165 col. 1 lines 6-15 and col. 2 lines 1-20 and page 166 lines 10-20. | 1-9, 13, 18, 20, 21, 22 |
| Y | DAVIS, W. C. et. al., " Use of the mannan receptor to selectively target vaccine antigens for processing and antigen presentation through the MHC class I and class II pathways", Annals of the New York Academy of Sciences, (2002 Oct) 969 119-25. See page 120 lines 15-33, and page 122 lines 11-25 | 1-9, 13-17, 21, 22, 26-31, 38 |

[X] Further documents are listed in the continuation of Box C [ ] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 10 December 2004 | 21 DEC 2004 |
| Name and mailing address of the ISA/AU | Authorized officer |
| AUSTRALIAN PATENT OFFICE<br>PO BOX 200, WODEN ACT 2606, AUSTRALIA<br>E-mail address: pct@ipaustralia.gov.au<br>Facsimile No. (02) 6285 3929 | **S.R. IDRUS**<br>Telephone No : (02) 6283 2659 |

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X, Y | AZZAM, T. et. al., " Dextran-spermine conjugate: An efficient vector for gene Delivery", Macromolecular Symposia (2003), 195(2002 IUPAC World Polymer Congress), 247-261<br>See page 248 line 29, page 250 line 16, and page 254 lines 1-6. | 1-9, 13, 18-22, 26 |
| P, X | KOZLOV I. A. et. al., "Efficient strategies for the conjugation of oligonucleotides to antibodies enabling highly sensitive protein detection", Biopolymers (2004 Apr 5) 73 (5) 621-30.<br>See in particular page 622 col. 1 line 50 to col. line 25, Fig. 3 page 625. | 1-9, 13, 22, 26 |
| A | VAUGHAN, H. A. et. al., " The immune response of mice and cynomolgus monkeys to macaque mucin 1- mannan", Vaccine (2000), 18(28), 3297-3309.<br>See whole document. | 1-49 |